REMARKS

A. Interview with the Examiner

Applicants thank the Examiner for the courtesy extended to Applicants' representative during a telephone interview on October 24, 2007. During the telephone interview, Applicants' representative discussed with the Examiner the claim rejections set forth in the July 27, 2007 office action, the currently pending claims, and possible amendments to the claims.

B. Status of the Claims

Claims 1-55 are pending, with claims 1-11, 42-46, and 52 currently under examination. Claims 12-41, 47-51, and 53-55 are currently withdrawn.

Claims 1 and 52, along with their corresponding dependent claims, are rejected under 35 U.S.C. § 112, ¶ 1 for allegedly containing new matter.

Claim 1-11, 42-46, and 52 are rejected under 35 U.S.C. § 112, ¶ 2, for allegedly being indefinite for failing to point out and distinctly claim the subject matter which Applicants regard as the invention.

Claims 1, 5, 6, 11, and 42-44 stand rejected under 35 U.S.C. § 102(b) for allegedly being anticipated by Michon et al. (In: Streptococci and the Host. (Ed) Horaud et al., Plenum Press, New York, pages 847- 850, 1997) (hereafter "Michon '97").

Claims 1, 2, 5, 6, 10, 11, and 42-44 are rejected under 35 U.S.C. § 102(b) for allegedly being anticipated by Paoletti et al. (Infect. Immun. 62:3234-3243, 1994) (hereafter "Paoletti").

Claims 9 and 52 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Paoletti, in view of Wang et al. (PNAS 95: 6584-6589, 1998) (hereafter "Wang").

Claims 2, 3, 7, 8, 45, and 46 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Michon '97, in view of U.S. Patent No. 6,602,508 (hereafter "Michon '508") and Laude-Sharp et al. (In: Abstracts of the 97th General Meeting of the American Society for Microbiology, Miami Beach, FL, page 251, #E-62, 1997) (hereafter "Laude-Sharp").

Claims 1-7 and 42-45 are rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 5,993,825 to Jennings ("Jennings"), in view of Paoletti and Claesson et al. (J. Pediatr. 114: 970199, 1989) (hereafter "Claesson").

C. Claim Amendments

In this paper, Applicants have amended claim 1 to clarify the invention. Claim 1 now recites the following:

> 1. A multivalent conjugate molecule comprising a carrier protein covalently linked to at least three different types of purified bacterial capsular polysaccharide,
>
> wherein each type of said at least three different types of purified bacterial capsular polysaccharide is obtained from a different serotype of a bacteria by treating the bacteria with an enzyme or base, directly followed by separation to isolate said at least three different types of purified bacterial capsular polysaccharide, and
>
> wherein the multivalent conjugate molecule elicits protective antibodies.

Support for this revised version of claim 1 is found throughout the specification. For example, support for "each type of polysaccharide…is obtained from a different serotype of a bacteria" is found in ¶ [02] ("the conjugate molecule [of the invention] provides immune protection against

multiple types of a particular bacteria in a single vaccine"), as well as ¶¶ [77] - [80] (showing isolation and purification of GBS polysaccharides from strains Ia, Ib, II, III, and V and subsequent conjugation to a Cβ protein]). Support for "a carrier protein covalently linked to at least three different types of purified capsular polysaccharide" finds support at ¶ [06] ("The present invention provides an immunogenic molecule comprising a carrier protein with at least three different bacterial capsular polysaccharides linked to the carrier protein"). Support for "treating the bacteria with an enzyme or base, directly followed by separation to isolate said at least three types of purified bacterial capsular polysaccharide" finds support at ¶ [56] (enzyme treatment to purify polysaccharides followed by separation of the polysaccharides with differential precipitation and chromatography) and ¶ [57] (base treatment to purify polysaccharide, followed by separation of the polysaccharides by ultrafiltration). Support for the phrase "the multivalent conjugate molecule elicits protective antibodies" finds support at ¶ [87] (showing that the conjugate molecule elicits a protective immune response).

Claims 2-4 and 6, which depend from claim 1, have also been amended so that the claim language contained in these claims is consistent with that of claim 1.

Claim 42 has been amended to clarify the invention. Specifically, claim 42 now specifies that the pharmaceutical composition comprises "multivalent conjugate molecule**s**." This amendment was made in response to the Examiner's remark during the October 24, 2007 telephone interview that she interpreted the previous version of claim 42 to contain only one multivalent conjugate molecule. Support for this amendment to claim 42 is found in the specification [e.g., see ¶ [67] ("The conjugate molecules of the invention are typically administered as a pharmaceutical composition in a pharmacologically acceptable carrier.") and

¶ [87] (showing that one dose for a CD1 female mouse is 1 μg of conjugated-type polysaccharide, which must contain more than one conjugate molecule).

Claim 52 has been amended to recite, inter alia, "purified polysaccharides having a molecular weight of 100 kilodaltons or less." Support for this amendment is found in the second sentence of paragraph [41], which describes the purified oligosaccharide as "substantially free of intact polysaccharide capsule, or fragments of it having a molecular weight above 100,000."

Applicants respectfully submit that no new matter has been added by these amendments.

D. Rejections under 35 U.S.C. § 102

1. Applicants' Claims Are Not Anticipated by Michon '97

Applicants respectfully traverse the rejection of claims 1, 5, 6, 11, and 42-44 under 35 U.S.C. § 102(b) for allegedly being anticipated by Michon '97. For the reasons set forth below, Applicants maintain that Michon '97 does not disclose the claimed conjugate molecules or the claimed pharmaceutical compositions containing such conjugate molecules. Accordingly, the rejection should be withdrawn. MPEP § 2131.

In a paper filed on April 23, 2007, Applicants noted that Michon '97 only describes type Ia, II, and III conjugates, wherein the type Ia, II, and III polysaccharides are all linked to different carrier protein molecules which may be of the same type. To support this statement, Applicants cited the first sentence of Section 3 of Michon '97:

> The GBS TT conjugates contained 79%, 68%, and 39% CPS by mass for the Ia, II, and III conjugates, respectively, while their beta C conjugate counterparts contained 81%, 53%, and 42% CPS by mass; the remaining mass is protein carrier.

Noting that this sentence refers to "conjugate**s**" and not a "conjugate", Applicants argued that the type Ia, II, and III conjugates are all separate and distinct molecules and the polysaccharides of these different serotypes are not attached to the same carrier protein, as recited in Applicants' claims.

In response, the Examiner explained that the term "carrier protein," which was recited in claim 1 and claim 42 without an indefinite article (i.e., "a"), suggested to the Examiner that the term "carrier protein…is not limited to the same carrier protein, but encompasses more than one carrier proteins [sic] of the same or different kind." [July 27, 2007 Office action, p. 4]. On this basis, the Examiner concluded that "Michon's (1997) multivalent conjugate vaccine is not excluded from the scope of the instant claims." [July 27, 2007 Office Action p.4].

However, Applicants' amended claim 1 specifies that the claimed multivalent conjugate molecule comprises a carrier protein that is covalently linked to at least three different types of purified bacterial capsular polysaccharide. In other words, the different types of purified bacterial capsular polysaccharide are covalently linked to the same carrier protein. Nowhere does Michon '97 describe such a multivalent conjugate molecule. At best, Michon '97 merely describes a mixture of monovalent conjugates.

Michon '97 does not disclose the conjugate molecules recited in claims 1, 5, 6, 11, and 42-44. Accordingly, Michon '97 does not teach all of the claim elements of Applicants' claims, and the § 102(b) rejection of these claims over Michon '97 should be withdrawn. MPEP § 2131.

2. Applicant's Claims 1, 2, 5, 6, 10, 11, and 42-44 Are Not Anticipated by Paoletti

Applicants respectfully traverse the rejection of claims 1, 2, 5, 6, 10, 11, and 42-44 under 35 U.S.C. § 102(b) as allegedly being anticipated by Paoletti. Paoletti does not disclose all of the claim elements of Applicants' claims. Accordingly, the rejection should be withdrawn. MPEP § 2131.

Paoletti is directed to a tetravalent GBS polysaccharide-tetanus toxoid conjugate vaccine. As noted in Applicants' previous response, Paoletti is similar to Michon '97 in that Paoletti does not disclose that different types of capsular polysaccharides can be conjugated to the same protein molecule. At best, Paoletti merely combines individual monovalent conjugates to produce a trivalent or a tetravalent vaccine [see Paoletti, page 3237, col. 1, last paragraph and page 3238, col. 2, first full paragraph].

Applicant's amended claims are directed to a multivalent conjugate molecule in which a carrier protein is "covalently linked to at least three different types of purified bacterial capsular polysaccharide," where each type of purified bacterial capsular polysaccharide is obtained from "a different serotype of a bacteria." Paoletti does not disclose such a conjugate molecule and thus does not anticipate Applicants' claims 1, 2, 5, 6, 10, 11, and 42-44.

Reconsideration and withdrawal of this ground of rejection are respectfully requested.

E. Rejections under 35 U.S.C. § 103

1. Applicants' Claims 9 and 52 Are Patentable over Paoletti and Wang

Applicants respectfully maintain their traversal of the rejection of claims 9 and 52 under 35 U.S.C. § 103(a) for allegedly being unpatentable over Paoletti, in view of Wang.

Briefly, the proposed combination of references fails to teach or suggest all of the elements of Applicants' claims. Accordingly, the rejection of these claims should be withdrawn. MPEP § 2143.

As noted above, Paoletti does not disclose a "multivalent conjugate molecule" as recited in Applicants' claims. At best, Paoletti merely describes the combination of individual monovalent conjugates in the preparation of trivalent or tetravalent vaccines.

Wang also does not teach or disclose the claimed multivalent conjugate molecules, a fact that the Examiner acknowledges ("The reference of Wang et al was not cited because it taught Applicants' multivalent conjugate vaccine, but was applied as a secondary reference…" [July 27, 2007 Office Action, page 6]).

Thus, Paoletti and Wang, whether taken alone or in combination, do not teach or suggest a "multivalent conjugate molecule" as claimed in Applicants' claims. Because the proposed combination of references fails to teach or suggest all of the claim elements of Applicants' claims, the rejection should be withdrawn. MPEP § 2143.

2. Applicants' Claims Are Patentable Over Michon '97, in view of Michon '508 and Laude-Sharp

Applicants respectfully traverse the rejection of claims 2, 3, 7, 8, 45, and 46 over Michon '97, in view of Michon '508 and Laude-Sharp. Briefly, none of the references, either alone or in combination, teach or suggest all of the claimed elements in Applicants' claims. Accordingly, the rejection under 35 U.S.C. § 103(a) should be withdrawn. MPEP § 2143.

As previously noted, Michon '97 does not teach or suggest Applicants' claimed multivalent conjugate, but instead only describes the combination of single polysaccharide-protein conjugates to form a multivalent vaccine.

Similar to Michon '97, Laude-Sharp also only describes a combination of monovalent conjugates. Laude-Sharp refers to a "trivalent combination vaccine, consisting of CPS-Cβ conjugates derived from CPS types Ia, II, and III". As Applicants noted previously, Laude-Sharp's reference to combining "conjugate**s**" to make the multivalent vaccine allows one to infer that even though the vaccine is trivalent, the conjugates themselves are not.

Michon '508 is directed to depolymerized Group B streptococcus type II and type III polysaccharides. As previously noted, Michon '508 "contemplates multivalent conjugates and their vaccines wherein different types of polysaccharides are conjugated to a single protein" [Michon '508, col. 9, lines 38-40]. The Examiner contends that the process steps recited in claims 1 and 42 do not distinguish Applicants' claimed conjugates from those of Michon '508.

Applicants respectfully disagree. Michon '508 does not teach or suggest Applicants' claimed multivalent conjugate. To prepare type II and type III Group B streptococcus polysaccharides, Michon '508 describes a depolymerization process that requires three steps: (1) base treatment; (2) nitrosation; and (3) separation. The nitrosation step leads to modified Group B streptococcus polysaccharides that contain a terminal 2,5-anhydro-D-mannose structure [see Michon '508, col. 6, Formulas I-IV]. These 2,5-anhydro-D-mannose structures are preserved during subsequent conjugation with protein, because conjugation only affects the aldehyde group on the 2,5-anhydro-D-mannose group:

> [t]he aldehyde group in the resulting 2,5-anhydro-D-mannose (Formula IV) residue formed at the reducing end of the polysaccharide fragment can be used directly, without further chemical manipulation (e.g., use of a spacer

> arm), for linking through reductive amination to an amino group containing polymer, preferably a protein [Michon '508, col. 6, lines 53-58].

[see also the chemical reactions set forth in cols. 8-9]. In contrast to Michon '508, Applicants obtain the claimed polysaccharide by treating the bacteria with an enzyme or base, directly followed by separation to isolate the polysaccharide. Because the instant claims do not require a nitrosation step, Applicants' polysaccharides do not contain a terminal 2,5-anhydro-D-mannose group. Thus, the polysaccharides of Michon '508 are structurally distinct from those of Applicants. Accordingly, the corresponding conjugates of Michon '508 are also structurally distinct from those of Applicants.

Applicants further note that Michon '508 actually teaches away from "treating the bacteria with an enzyme or base, directly followed by separation." As mentioned in the previous response, Michon '508 teaches away from the use of enzymes by describing enzymatic methods as "costly" [Michon '508, col. 2, line 11].

On the basis of the foregoing, Applicants respectfully maintain that Michon '508, like Michon '97 and Laude-Sharp, also does not teach or suggest Applicants' claimed multivalent conjugates.

Because all of the cited references, whether considered alone or in combination, fail to teach or suggest all of the claim elements of Applicants' invention, the rejection of claims 2, 3, 7, 8, 45, and 46 should be withdrawn. Applicants respectfully request reconsideration and withdrawal of the rejection of these claims.

3. Applicants' Claims Are Patentable Over Jennings, in view of Paoletti and Claesson

Applicants respectfully maintain their traversal of the rejection of claims 1-7 and 42-45 under 35 U.S.C. § 103(a) for allegedly being unpatentable over Jennings, in view of Paoletti and Claesson. None of these references, alone or in combination, teach or disclose Applicants' claimed multivalent conjugate. Accordingly, the rejection should be withdrawn. MPEP § 2143.

As noted in the previous response, Jennings merely describes multivalent vaccines that are prepared by combining conjugate molecules that have only one type of polysaccharide attached to a protein component. According to Jennings,

> this invention claims multivalent vaccines comprising the conjugate **molecules** of the invention and **at least one other immunogenic molecule** capable of eliciting the production of antibodies to a pathogenic substance other than Group B streptococcus type II or type V. In particular, in addition to comprising the GBS type II and/or GBS type V conjugate **molecules**, the multivalent vaccine, according to the invention, further comprises **other immunogenic molecules** capable of eliciting the production of antibodies to pathogens selected from the group consisting of Group B streptococcus types Ia, Ib, III, IV and Haemophilus influenzae type b and E. coli type K1 [Jennings, col. 2, lines 53-65 (emphasis added)].

Similarly, Paoletti is only limited to combinations of monovalent conjugates, as discussed above. Claesson does not alleviate the deficiencies of Jennings or Paoletti, because Claesson does not teach or suggest the claimed multivalent conjugate either. At best, Claesson merely describes a Hib-TT conjugate that contains only one type of polysaccharide attached to a protein carrier.

Because all of the cited references, whether considered alone or in combination, fail to teach or suggest all of the claim elements of Applicants' invention, the rejection of claims

1-7 and 42-45 should be withdrawn. Applicants respectfully request reconsideration and withdrawal of the rejection of these claims.

F. Rejections Under 35 U.S.C. § 112

1. Rejection of Claim 1 Under 35 U.S.C. § 112, ¶ 1 (new matter)

The Examiner rejected the version of claim 1 presented in the previous response for allegedly incorporating new matter. In making this rejection, the Examiner stated that "while the recited at least three different types of bacterial capsular polysaccharide are required to be purified, the covalently linked polysaccharides that comprise these at least three different types of bacterial capsular polysaccharide can be unpurified." [July 27, 2007 Office Action, page 9].

Without agreeing to the propriety of this rejection, Applicants respectfully submit that this rejection is moot in view of the amendments that have been made to claim 1.

2. Rejection of claim 52 Under 35 U.S.C. § 112, ¶ 1 (new matter)

The Examiner rejects claim 52, contending that there is no support for "purified polysaccharides that are less than 100 kilodaltons in molecular weight." In making this rejection, the Examiner states that "[n]ew matter includes not only the addition of wholly unsupported subject matter but also, adding specific percentages or compounds after a broader original disclosure…"

Applicants respectfully disagree with this rejection, because the claimed range in amended claim 52 is fully supported by the specification. As noted in the previous office action, paragraph [41] of the specification states that "purified oligosaccharide, or bacterial capsule polysaccharide, is substantially free of intact polysaccharide capsule, or fragments of it having a

molecular weight above 100,000." In other words, the specification states that purified polysaccharides have a molecular weight of 100 kilodaltons or less, which is what is claimed in amended claim 52.

Applicants further note that there is no requirement that a claim term be supported by the specification using the exact words of the claim term. Indeed, stating that purified polysaccharides have a molecular weight of 100 kilodaltons or less is equivalent to stating that the purified polysaccharides are "substantially free of …fragments…having a molecular weight above 100,000."

For these reasons, reconsideration and withdrawal of this ground of rejection are respectively requested.

3. Rejections Under 35 U.S.C. § 112, ¶ 2

In view of the amendments to claims, Applicants respectfully assert that the rejections set forth in items (a) - (d), and (f)-(i) on page 11 of the July 27, 2007 Office Action are now moot.

With respect to item (e), the Examiner rejects claims 2-4 under 35 U.S.C. § 112, stating that it is unclear whether the bacterial capsular polysaccharides recited in claims 2-4 are different from or in addition to those in base claim 1. In response, Applicants respectfully assert that these claims, as amended, clearly define the total number of types of purified bacterial capsular polysaccharide found in each multivalent conjugate molecule.

On the basis of the foregoing amendments are remarks, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1-11, 42-46, and 52 under 35 U.S.C. § 112, ¶ 2.

CONCLUSION

Based on the foregoing amendments and remarks, Applicants respectfully request reconsideration and withdrawal of the rejection of claims and allowance of this application.

AUTHORIZATION

The Commissioner is hereby authorized to charge any additional fees which may be required for consideration of this Amendment to Deposit Account No. 50-3732, Order No. 13564-105038US1.

In the event that an extension of time is required, or which may be required in addition to that requested in a petition for an extension of time, the Commissioner is requested to grant a petition for that extension of time which is required to make this response timely and is hereby authorized to charge any fee for such an extension of time or credit any overpayment for an extension of time to Deposit Account No. 50-3732, Order No. 13564-105038US1.

Respectfully submitted,
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Dated: October 29, 2007

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